REMARKS

Pending Claims:

In this application, claims 31-38 are currently pending.

Double Patenting

Applicant notes that the Examiner has made a provisonal rejection for obviousness type double patenting. Upon the indication of otherwise allowable claims the applicant will file a terminal disclaimer based upon the supposition that allowable claims will be viewed as "obvious" in view of the original and issued claims.

Rejection under 35 U.S.C. §112 (paragraph 1)

In the Office Action, a rejection was made under 35 U.S.C: §112 (paragraph 1) to claims 31 – 38. In the Examiners view thee claims are not supported by the specification. The applicants set forth a concordance between the claim language and the specification. As an aid to this analysis the applicants use the column and line numbers of the issued US Patent 5,190,744, which represent the earliest disclosures of the invention.

Claim 31

The language "thereby collecting temporally spaced sets of 3-D and 2-D data, each data set collected serially throughout an acquisition or collection time; comparing 3-D and 2-D data from temporally spaced set of data by evaluating 2-D or 3-D temporally acquired images to assess the blood flow or angiographic abnormality or variation" is intended to provide a generic identification of the process described inter alia at column 6 lines 53 through line 62. Please note that pixel data described at line 59 is inherently 2-D while the voxel data is inherently 3-D. The comparison process is commented on below.

Support of the use of the process in blood flow or angiographic settings is supported by the discussion on Col 2 at lines 33 through 35 where coronary ischemia is specifically recited (recall that the coronary artery system is on the heart).

Temporal collection of image data is discussed throughout the specification but applicant notes the discussion in column 2 at lines 14 through 24 is clear support of the claim limitations.

Claim 32- 36

This claim requires a physician in the process. Please note that the process is described on column 7 at lines 15 et seq refer to "including display of zones of reduced or enhanced perfusion optionally superimposed on a selected background image". Although the statement is silent on the presence of a physician the intent of the process is to aid diagnostic evaluation of the images. The display referred to in this statement is "to" the attending physician.

Claim 34- 35

This claim calls for time periods discloses in the summary of the invention at column 2 on lines 16 – 24., which set forth the range of acceptable values and the motivation for selecting the enumerated time intervals. The longer time intervals in the claims are supported by the non limiting but illustrative experimental values recited for example in column 7 at line 36 through 46.

Claim 36

The claim is amended to clarify that the claim further refines the " MR technique" limitation in claim 31. It is the intention of this claim to capture the best modalities used in the Examples recited in the specification.

Claim 37-38

This inclusion of single shot imaging sequence is supported by the discussion of comparing a contrast enhanced image with an image taken before the administration of contrast agent. See for example column 7 lines 9 and 10.

Rejection under 35 U.S.C. §112 (paragraph 6)

The Examiner notes that the terms OR and AND are both used in claim 31 and claim 33 and may give rise to confusion as to claim scope. In general the claims seems accurate to the applicants. It is the intention to use the term "OR" in the inclusive rather

than exclusive OR sense. Both 2-D and 3-d data are taken and either one type or the other or both types may be used for analysis. If alternate language makes this more explicit applicant will amend to clarify the issue but the applicants are of the view that the present language is compact and explicit and accurate as presented.

CONCLUSION

All of the claims remaining in this application should now be seen to be in condition for allowance. The prompt issuance of a notice to that effect is solicited.

Respectfully submitted,
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CLAIMS and their STATUS

1. (canceled) A method of detecting blood flow abnormality or variation in a human body, said method comprising the steps of:

administering into the vasculature of said body a timed injection of a contrast enhancing amount of paramagnetic metal containing magnetic resonance imaging contrast agent;

subjecting said body to a magnetic resonance imaging procedure capable of generating from magnetic resonance signals from said body a series of temporally spaced images of at least a part of said body into which said agent passes, said procedure being a high speed or single shot imaging procedure;

detecting temporal variations in said images to identify regions of abnormality to provide an indication of the degree of blood flow abnormality.

2. (canceled) A method according to claim 1 wherein said contrast agent comprises a physiologically tolerable chelate complex of a paramagnetic lanthanide ion or a physiologically tolerable salt of such a chelate.

3. (canceled) A method according to claim 2 wherein said contrast agent is a chelate complex of a metal ion selected from the paramagnetic ions of Yb, Tm, Dy, Ho, Er and Gd, or a physiologically tolerable salt thereof.

4. (canceled) A method according to claim 3 wherein said contrast agent is a chelate complex of Dy(III) or a physiologically tolerable salt thereof.

5. (canceled) A method according to any one of claims 1 to 4 wherein said contrast agent comprises a physiologically tolerable non-ionic paramagnetic lanthanide chelate complex.

6. (canceled) A method according to any one of claims 2 to 5 wherein said chelate complex is a complex of a linear, branched or macrocyclic chelant selected from polyaminopolycarboxylic acid chelants and from chelants wherein

one or more carboxylic acid groupings are replaced with an amide, ester or hydroxamate grouping.

7. (canceled) A method according to claim 6 wherein said chelate complex is a complex of a chelant selected from the group consisting of DTPA, DTPA-BMA, DOTA, DO3A, DTPA-BMO and Hp-DO3A.

8. (canceled) A method according to claim 2 wherein said chelate complex is DyDTPA-BMA.

9. (canceled) A method according to any one of claims 1 to 8 wherein said contrast agent is administered at a dosage of 0.02 to 3 mmol/kg bodyweight.

10. (canceled) A method according to claim 9 wherein said contrast agent is administered at a dosage of 0.08 to 0.5 mmol/kg.

11. (canceled) A method according to any one of claims 1 to 10 wherein said procedure is one having an image acquisition time of less than 0.5 seconds.

12. (canceled) A method according to any one of claims 1 to 13 wherein said procedure is an echo planar imaging procedure.

13. (canceled) A method according to any one of claims 1 to 12 wherein administration of said contrast agent is by bolus injection.

14. (canceled) A method according to any one of claims 1 to 10 comprising generating temporally spaced T_2^* or T_2- weighted images.

15. (canceled) A method according to claim 14 wherein said magnetic resonance imaging procedure is a spin-echo or gradient echo procedure.

16. (canceled) A method according to either of claims 14 and 15 comprising generating and comparing T_1-weighted images or signals transformable thereto

and T_2^* or T_2-weighted images or signals transformable thereto whereby to identify body regions in which blood perfusion occurs.

17. (canceled) A method according to any one of claims 1 to 16 being a method of detecting body regions of blood flow deficit.

18. (canceled) A method according to claim 17 being a method of detecting ischemic regions.

19. (canceled) A method according to claim 17 being a method of detecting body regions in which blood perfusion is surgically, thermally or chemically modified.

20. (canceled) A method according to claim 1 wherein said contrast agent comprises a physiologically tolerable complex of a paramagnetic transition metal ion or a physiologically tolerable salt of such a chelate.

21. (canceled) A method of detecting and evaluating the severity of blood flow abnormality in a human body, said method comprising the steps of:

administering into the vasculature of said body a contrast enhancing amount of a paramagnetic metal containing magnetic resonance imaging contrast agent;

subjecting said body to a magnetic resonance imaging procedure capable of generating from magnetic resonance signals from said body a series of temporally spaced images of at least a part of said body into which said contrast agent passes, said procedure being a fast, high speed or single shot imaging procedure, to detect temporal variations in said magnetic resonance signals or images;

detecting blood flow abnormality or flow variation in obstructed blood vessels in said body; and

identifying from said temporal variations in said images the blood flow abnormality.

22. (canceled) A method of monitoring the vasodilatory or vasoconstrictive effects of a physiologically active substance administered to a human or non-human animal body said method comprising administering said substance into said body, administering into the systemic vasculature of said body a contrast enhancing amount of an intravascular paramagnetic metal containing magnetic susceptibility magnetic resonance imaging contrast agent, subjecting said body to a magnetic resonance imaging procedure capable of generating from magnetic resonance signals from said body a series of temporally spaced images of at least a part of said body into which said agent passes, and detecting temporal variations in said signals or images whereby to monitor the vasoconstriction or vasodilation induced by said substance.

23. (canceled) A method of monitoring surgically induced blood perfusion variations said method comprising administering a contrast enhancing amount of an intravascular paramagnetic metal containing mass magnetic susceptibility magnetic resonance imaging contrast agent into the systemic vasculature system of a human or animal body which is undergoing or has undergone surgery, subjecting said body to a magnetic resonance imaging procedure capable of generating from magnetic resonance signals from said body a series of temporally spaced images of at least a part of said body into which said agent passes, and detecting temporal variations in said signals or images whereby to identify regions of surgically induced variations in blood perfusion.

24. (canceled) A method as claimed in any one of claims 1 to 23 wherein said contrast agent is administered as a contrast medium composition comprising DyDTPA-BMA and CaNaDTPA-BMA in a molar ratio of about 20:1.

25. (canceled) The use of a paramagnetic metal containing compound for the manufacture of a contrast agent composition for use in a method as claimed in any one of claims 1 to 24.

26. (canceled) Use as claimed in claim 25 of DyDTPA-BMA.

28. (canceled) A method according to claim 1 wherein said human body includes blood vessels.

29. (canceled) A method according to claim 1 wherein said timed injection includes bolus injection into a blood vessel.

30. (canceled) The method of claim 28 including the step of:

detecting blood flow abnormality or flow variation resultant from obstructed blood vessels.

31. (renumbered)A method of detecting blood flow or angiographic abnormality or variation in a vessel or tissue comprising:

administering a contrast enhancing amount of a paramagnetic metal containing magnetic resonance (MR) contrast agent into a vessel;

imaging a least a portion of the body through which the MR contrast agent passes, with a MR imaging technique, thereby collecting temporally spaced sets of 3-D and 2-D data, each data set collected serially throughout an acquisition or collection time;

comparing 3-D and 2-D data from temporally spaced set of data by evaluating 2-D or 3-D temporally acquired images to assess the blood flow or angiographic abnormality or variation.

32. (renumbered)The method of claim 1 wherein said comparing step is carried out by a physician visually examining at least two time sequenced images.

33. (renumbered)The method of claim 1 wherein said comparing step is carried out by software quantitatively manipulating 3-D or 2-D data from at least two temporally spaced sets of data.

34. (renumbered)The method of claim 1 wherein said collection time is

greater than about 60 milliseconds.

35. (renumbered)The method of claim 1 wherein said collection time is less than about 15 seconds.

36. (renumbered)The method of claim 1 wherein said MR imaging [process] technique is selected from the group:

T2* weighted, T2 weighted, T1 weighted imaging sequences.

37. (renumbered)A method of detecting blood flow abnormality or variation, in a human body, said method comprising the steps of:

administering into the vasculature of said body a timed injection of a contract enhancing amount of a paramagnetic metal containing magnetic resonance imaging contrast agent,

subjecting said body to a magnetic resonance imaging procedure capable of generating from magnetic resonance signals from said body a series of temporally spaced images of at least part of said body into which said agent passes, said procedure being a fast, high speed or single shot imaging procedure,

detecting temporal variations in said signals or images; and from said temporal variations identifying regions of abnormal or modified blood flow in said body and providing a quantitative indication of the degree of blood flow abnormality.

38. (renumbered)A method of detecting and quantitatively evaluating the severity of blood flow abnormality in a human body, said method comprising the steps of:

administering into the vasculature of said body a contrast enhancing amount of a paramagnetic metal containing magnetic resonance imaging contrast agent;

subjecting said body to a magnetic resonance imaging procedure capable of generating from magnetic resonance signals from said body a series of temporally spaced images of at least a part of said body into which said contrast agent passes, said procedure being a fast, high speed or single shot imaging

procedure, to detect temporal variations in said magnetic resonance signals or images;

detecting blood flow abnormality or flow variation in obstructed blood vessels in said body; and

identifying from said temporal variations in said images the blood flow abnormality.